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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/737,544	12/18/2000	Mark B. Pepys	P 0275486 / 201045/JND	1521

909 7590 06/29/2006

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EXAMINER	
WANG, SHENGJUN	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/737,544	PEPYS, MARK B.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-15,17-25 and 42-56* is/are pending in the application.

4a) Of the above claim(s) *4-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,10-15,17-25 and 42-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments, remarks and the declarations under 37 CFR 1.131 and 1.132 is acknowledged.

Several topographic error in the prior office action are noted. It is noted that applicants elected atherosclerosis as elected species of condition being treated, and hexadecyl phosphorylcholine as the species of phosphocholine (response filed August 29, 2003). The claims have been examined insofar as they read on the elected species. Claims 4-9, directed to conditions other than atherosclerosis, have not been examined, and have been with drawn from further consideration as drawn to non-elected species. Claims 4-9 should not be listed as rejected claims in the prior office action. Also the rejections under 35 U.S.C. 112 are applicable to all the examined claims.

Claim Rejections 35 U.S.C. 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-2, 10-15, 17-25, 42-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating atherosclerosis (see pages 20-37 of the specification herein), does not reasonably provide enablement for preventing atherosclerosis, and for treating and/or preventing of tissue damage in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

3. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ 2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factor to consider when assessing if a disclosure would have required undue experimentation. The court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

The claims are directed to treating and/or preventing tissue damage. "tissue damaging" herein essentially reads on all disorders, including, atherosclerosis, cancers, Alzheimer's disease, viral infections. The state of the art in treating such diseases is low. There is no established method for preventing such disease in the art. It is known it the art that excess amounts of human CRP would induce myocardial infarction, markedly increases morbidity, mortality and the infarct size in animal model (Griselli et al.). Applicant provides evidence showing that, in the same model, CRP inhibitor would suppress the pathogenic effect of CRP. (pages 20-35 herein). The specification provide no further guidance, direction or working examples as how the claimed method would be effective in preventing atherosclerosis, no does it provide guidance, direction

or working examples for treating and preventing other tissue damage. The underline etiology of atherosclerosis, as well as other diseases associated with tissue damaging (cancers, Alzheimer, etc), are complex and unclear. The art and the instant application have shown that excess amount of CRP may cause tissue damage. However, there is no evidences that CRP is solely response for causing tissue damage. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed of physiological activity. The instant claims read on preventing and/treating preventing and/treating all diseases associated with tissue damage, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention, absent undue experimentation.

Claim Rejections 35 U.S.C.§ 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1, 2, 10-15, 17-25 and 42-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhakdi et al. (IDS) and Kitao, in further view of Yedgar et al. (US 5,064,817) and Wissner et al. (US 4,640,913).

3. Bhakdi et al. and Kitao teaches that phosphorylcholine are useful for inhibiting the binding of CRP to LDL, wherein the binding of CRP to LDL is known to be a factor of atherosclerosis. See the abstracts.

4. The primary references do not teach expressly the employment of hexadecyl phosphorylcholine for treating atherosclerosis.

5. However, Yedgar et al. teaches that various phosphorylcholine derivatives are known to be useful for treating pathological conditions including atherosclerosis. See, particularly, column 13, lines 22-38, and the claims. Wissner et al. teaches various phosphorylcholine derivatives are useful for treating hypertension, an underline etiology of atherosclerosis. See, particularly, the abstract, column 1, lines 19-26, and the claims.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ a phosphorylcholine compound, such as hexadecyl phosphorylcholine, for treating atherosclerosis.

A person of ordinary skill in the art would have been motivated to employ a phosphorylcholine compound, such as hexadecyl phosphorylcholine, for treating atherosclerosis because phosphorylcholine is known to inhibiting the binding of CRP to LDL is known to be a factor of atherosclerosis, suggesting the usefulness of phosphorylcholine for treating atherosclerosis, and a ester, or salt of an active therapeutical compound, would have considered, an equivalent of the active therapeutical compound. Further, phosphorylcholine derivatives are generally known to be useful for treating atherosclerosis. With respect to stroke, note, a method known to be useful for treating the underline etiology of a disorder would have been reasonably expected to be useful for treating or preventing the disorder.

Response to the Arguments

Applicants' amendments, remarks, and the declarations under 37 CFR 1.131 and 1.132 have been fully considered.

6. The declaration filed on March 2, 2006 under 37 CFR 1.131 is sufficient to overcome the Yeh reference.

7. The Katz type declaration filed on March 2, 2006 is sufficient to overcome the Griselli reference.

8. However, the amendments, remarks, and the declarations are not sufficient to over come the rejections set forth above.

Respect to the rejections under 35 U.S.C. 112, the examiner reiterates that "The claims are directed to treating and/or preventing tissue damage. "tissue damaging" herein essentially reads on all disorders, including, atherosclerosis, cancers, Alzheimer's disease, viral infections. The state of the art in treating such diseases is low (the newly added limitations do not exclude any of those disease). There is no established method for preventing such disease in the art. The examiner recognizes that "It is known it the art that excess amounts of human CRP would induce myocardial infarction, markedly increases morbidity, mortality and the infarct size in animal model (Griselli et al.). Applicant provides evidence showing that, in the same model, CRP inhibitor would suppress the pathogenic effect of CRP. (pages 20-35 herein)." However, The specification provide no further guidance, direction or working examples as how the claimed method would be effective in preventing atherosclerosis, no does it provide guidance, direction or working examples for treating and preventing other tissue damage. Further, there is no evidence showing that phosphocholine would actually completely prevent the pathogenic effect of CRP. It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

As to the rejections under 35 U.S.C. 103, it is noted that the "factor" mentioned is indeed a pathogenic factor. Applicants contend that the cited references, as well as the art in general, merely have speculation that CRP is a pathogenic factor for atherosclerosis, and "present no evidence that CRP promotes or causes atherogenesis in any way, or has any pathological effect on tissue lesions." The arguments are untenable. Particularly, prior art suggested that CRP is a pathogenic fact for atherosclerosis, and phosphocholine has been known to be highest affinity small molecule ligand for CRP. It would have been obvious to one of ordinary skill in the art, at the time the claimed invention was made, to employ phosphocholine as a CRP antagonist for alleviate the pathogenic effect. Applicant's further confirmation of what has been suggested by the prior art would not make the suggested subject matter patentable.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHENGJUN WANG
PRIMARY EXAMINER

Shengjun Wang
Primary Examiner
Art Unit 1617